Remarks

Claims 1-24, and 26-25 are pending in the instant application, and claims 7-14, 23, 24, and 26-28 are under consideration. Claims 1-45 are herein cancelled, and new claims 46-60 are added. Support for the newly added claims can be found in the original claims and in the specification as originally filed.

Formal Matters

Amendment in Paper No. 8

The Examiner notes that the amendment in Paper No. 8 has not been entered because the amendment does not correspond to the specification. Applicants have reviewed the specification and have discovered that the pagination referred to in Paper No. 8 is indeed incorrect, and thank the Examiner for his efforts in clarifying the inaccuracy in the page references. Applicants submit that they have amended the specification herein to correctly reflect the page and paragraphs referenced by the amendment, and request that these amendments be entered into the application.

Rejection of Claims 7-14, 23, 24, and 26-28 Under 35 U.S.C. §101

The Examiner has rejected the claims under 35 U.S.C. §101 as being drawn to an invention which is not supported by either a well established utility or an asserted specific, substantial, and credible utility. The Examiner asserts that, even though the specification teaches that (1) GPR86 is a receptor for ADP, a molecule with well established physiological roles in numerous biological systems, (2) ADP transduces cellular signalling events via GPR86 including activation of IP_3, adenylyl cyclase, and MAP kinase cascades (ERK1 and 2 phosphorylation), (3) GPR86 is a member of a well established family of adenine nucleotide G-protein coupled receptors, (4) GPR86 has a tissue distribution which is consistent for its role in physiological processes, including immune processes, and (5) the interaction of ADP with GPR86 can be used as the basis for the identification of compounds for the modulation of the ADP/GPR86 interaction, the specification does not teach the "physiological significance" of the GPR86 receptor and thus does not meet the utility requirement. Applicants submit that the rejected claims have been cancelled herein, however, to the extent that the Examiner considers the

rejection to apply to newly added claims 46-60, Applicants submit respectfully that the Examiner has set improperly the hurdle of the utility requirement at an elevated height which is far more stringent that that set out by the Patent Office's own utility guidelines.

The Utility Examination Guidelines (Fed. Reg. 66, 2001, p. 1092) clearly articulate that if the applicant has asserted that the claimed invention is "useful for **any particular practical purpose** (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility". The guidelines go on to explain the meaning of specific and substantial describing that the requirement excludes "throw away", "insubstantial" or "nonspecific" utilities, "such as the use of a complex invention as landfill". The guidelines indicate that credibility is to be judged from the perspective of one of ordinary skill in the art, and that Applicants need only provide one credible assertion of a specific and substantial utility to meet the requirement. Applicants submit that the teaching of GPR86 transducing the cellular signal of a well established transmitter (ADP), combined with the tissue distribution, and membership in a well established family of receptors meet the relatively low bar set by the utility guidelines.

The Examiner has articulated repeatedly, however, that in order to satisfy the utility requirement, Applicants are required to present evidence of the asserted utility of the GPR86 receptor. The Examiner indicated to Applicants representative in an informal telephone conversation on January 12, 2004, that to satisfy the utility requirement, in addition to the asserted utility provided in the specification, Applicants could provide additional data which supports the asserted utility, either in the form of a post-filing scientific publication, or Applicants' additional laboratory data. For example, where the specification teaches that the GPR86 receptor, based on its tissue distribution may play a role in immune function, the Examiner has indicated that Applicants may provide evidence, either via a post-filing publication, or supplemental data from the inventors which corroborates the utility asserted by Applicants as of the application filing date. Without acquiescing to either the rejection or the Examiner's interpretation of the utility requirement under 35 U.S.C. §101, Applicants nevertheless submit herewith the Rule 132 Declaration of Dr. Jean-Marie Boeynaems, one of the inventors of the present invention, which provides further experimental evidence to confirm the well established and asserted utilities of the GPR86 receptor.

The specification teaches, *inter alia,* that one utility of the present invention is the physiological role of GPR86 in immune functionality, based on its tissular distribution in cells of the lymphocytic lineage. The Rule 132 Declaration shows that, consistent with the teachings of the specification and assertions made by Applicants during the prosecution of this application, the GPR86 receptor transduces a physiological signal mediated by ADP. Specifically, the data provided in the declaration shows that ADP induces the phosphorylation of ERK1 in human dendritic cells. The phosphorylation can be blocked by the application of the GPR86 receptor antagonist AR-C69931MX. The Declaration also shows that in mouse dendritic cells, AR-C69931MX potentiates the production of IL-12 in response to CD40 ligand stimulation, indicating that GPR86 plays an inhibitory role in IL-12 cytokine production. This data is consistent with the teaching in the specification at page 43, lines 17-21 that "GPR86, which is expressed in cells of the lymphocyte lineages...spleen as well as leukemic cells, can have a role in immune processes". Applicants respectfully submit that even the unusually high utility hurdle set by the Examiner should be cleared by the evidence presented in the Rule 132 Declaration which corroborates Applicants' both the well established and asserted utility provided in the specification.

Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

Rejection of Claims 7-14, 23, 24, and 26-28 Under 35 U.S.C §112, First Paragraph

The Examiner has rejected claims 7-14, 23, 24, and 26-28 under 35 U.S.C. §112, first paragraph for lack of enablement. The Examiner asserts that since the claimed invention does not have either a well established utility or an asserted utility which is specific, substantial and credible, that the specification could not have taught one of skill in the art how to make and use the invention without undue experimentation.

Applicants submit that they have successfully rebutted the Examiner's rejection above for lack of utility, thus obviating the Examiner's rejection under §112, first paragraph for lack of enablement. Applicants submit that the specification provides ample guidance to permit one of skill in the art to practice the claimed invention without the need to resort to undue experimentation. Applicants accordingly request that the rejection be reconsidered and withdrawn.

Rejection of Claims 7-14, 23, 24, and 26-28 Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected the claims as indefinite because the term "GPR86" is not defined unambiguously in the specification. The Examiner asserts that the teaching in the specification that "The present invention is related to the GPR86 ($P2Y_{13}$) receptor (or any homologous sequence), the nucleic acid sequence of which is set forth in SEQ ID NO: 1 and the amino acid sequence of which is set forth in SEQ ID NO: 2" is ambiguous because it encompasses homologous sequences of GPR86. Applicants respectfully disagree with the Examiner.

One of the primary purposes of the requirement for definiteness under 35 U.S.C. §112, second paragraph, is to ensure that the claims of an issued patent serve the notice function required by the law. See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000). The key question then is whether the scope of the invention can be determined by the language used in the claims. Applicants also note that the breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689 (CCPA 1971). Moreover, the Manual of Patent Examining Procedure states that the Examiner "should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness" (MPEP 2173.02; emphasis in original).

As noted by the Examiner, the claims recite "GPR86" and the specification teaches that the invention relates "to the GPR86 ($P2Y_{13}$) receptor (or any homologous sequence), the nucleic acid sequence of which is set forth in SEQ ID NO: 1 and the amino acid sequence of which is set forth in SEQ ID NO: 2". The teachings of the specification do not end there, however. The next paragraph of the specification teaches that a homologous sequence means a sequence which "presents a high sequence identity (more than 70%, 75%, 80%, 85%, 90%, 95%, or 98% sequence identity) with the complete human nucleotide or amino acid sequence...and is preferably characterized by the same pharmacology, especially preference for binding to ADP>>IDP>UDP". Thus, the specification teaches that a homologous sequence of GPR86 is one which as at least 70% sequence identity to the sequence of GPR86 recited in the sequence listing, and which retains the same pharmacology and ligand binding properties as the GPR86 receptor sequence of SEQ ID NO: 2, or which is encoded by the nucleotide sequence of SEQ ID

NO: 1. With respect to the percent identity between the expressly recited GPR86 sequence and potential homologs, the specification teaches methods which may be used by one of skill in the art to determine both the degree of sequence identity (page 18, line 23 – page 23, line 11) and the ligand binding characteristics of a GPR86 receptor homolog (page 26-44). Thus, given the teachings in the specification, Applicants submit that one of skill in the art would be put sufficiently on notice as to whether they infringed claims 7-14, 23, 24, and 26-28, because the skilled artisan would be able to readily determine whether a particular receptor was a GPR86 receptor or a homolog thereof, as described in the specification. Applicants thus submit that the claims are definite and that the scope of the claims has far more than a "reasonable degree" of clarity.

Nevertheless, in order to expedite the prosecution of this application, and while not acquiescing to the Examiner's rejection, Applicants have cancelled the rejected claims and submitted herewith new claims 46-60 which recite, where appropriate, SEQ ID Nos which are representative of the recited GPR86 polynucleotide and polypeptide molecules. Applicants thus, submit that the Examiner's rejection is now moot, and request that it be withdrawn.

The Examiner has also rejected claim 23 as indefinite because the measuring of the binding of an agent to GPR86 does not necessarily identify an agent that modulates the function of GPR86. Applicants respectfully disagree with the Examiner. Applicants submit that claim 23 has been cancelled. The scope of the invention encompassed by claim 23, however, is now provided by new claims 48 and 50, which clearly set forth the method steps which one of skill in the art would follow to identify a compound which modulates the signaling activity of GPR86. Applicants request accordingly that the rejection be reconsidered and withdrawn.

Conclusion

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

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